REMARKS

This Response is in reply to the Notice of Non-Compliant Amendment dated July 19, 2005. In the Office communication, entry of the Preliminary Amendment dated January 12, 2005, was denied. The Office communication now requires Applicants to address the rejections made of record in the Office Action dated January 27, 2005. Claims 6, 23 to 27 and 31 to 35 are, therefore, pending in the application. Claims 26 and 27 have been cancelled. Claims 6, 23, 25, 31 and 33 have been amended. New Claims 39 to 80 have been added. No new matter has been added by these amendments or new claims. A Petition for a two-month extension of time is submitted herewith. A check in the amount of $400.00 is submitted herewith to cover the cost of the two-month extension and the balance of the fee for the new claims submitted in addition to the new claims presented in the Preliminary Amendment. Please charge Deposit Account No. 02-1818 for any insufficiency or credit the account for any overpayment.

In the Office Action, Claim 6 was rejected under 35 U.S.C. §112, second paragraph, as being dependent on cancelled Claim 1. Accordingly, Claim 6 has been amended to be in independent form and the rejection has, therefore, been overcome.

In the Office Action, Claims 6, 23, 25 to 27, 31 and 33 to 35 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Nakafuku et al. ("*Nakafuku*"). Applicants respectfully traverse these rejections for at least the reasons discussed below.

Of the rejected claims, Claims 6, 23, and 31 are the only independent claims. Claim 6 has been amended and is directed to a cell culture comprising, among other elements, a neural precursor cell line, wherein at least about 20% of the cell line is capable of differentiating into neurons upon withdrawal of mitogen. Support for this amendment can be found in the Specification at, for example, pages 10 and 19.

In addition, Claim 23 has been amended to provide a cell culture comprising, among other elements, mammalian neural precursor cells, wherein at least about 20% of the mammalian neural precursor cells is capable of differentiating into neurons upon withdrawal of mitogen. Support for this amendment can be found in the Specification at, for example, pages 5, 10 and 19. Therefore, no new matter has been added by these amendments.

Nakafuku fails to disclose a neural precursor cell line wherein at least about 20% of the cell line is capable of differentiating into neurons as recited in the claimed invention. In contrast to the claimed invention, *Nakafuku* discloses that, even under optimal conditions, i.e. addition of β-E_2 and bFGF in a suspension culture, only 12% of the cells described in *Nakafuku* are capable of differentiating into neurons. *Nakafuku*, page 162, right column, and Table I. Furthermore, *Nakafuku* does not disclose a cell line of mammalian neural precursor cells wherein the cells differentiate upon withdrawal of mitogen and the receptor ligand as recited in Claims 6 and 23. In fact, *Nakafuku* states that only 0.3% of the MNS-57 cell line differentiate into neurons in the absence of bFGF and β-E_2 . To this end, the MNS-57 cell line in *Nakafuku* require bFGF and *c-myc* activation by estrogen for differentiation of the cells as described on pages 162-163 and in Table 1 of *Nakafuku*. Therefore, for at least these reasons, Applicants respectfully submit that *Nakafuku* fails to teach or disclose the claimed invention.

Nakafuku does not disclose a cell culture comprising a cell line of mammalian neural precursor cells, produced by, among other elements, culturing the neural precursor cells in a serum-free medium and in the presence of a first mitogen as recited in Claim 31. In contrast to the claimed invention, *Nakafuku* supplements the culture media with serum to proliferate cells. As described on page 155 of *Nakafuku*, the cells are grown in culture medium including 10% fetal bovine serum both before and after transfection with the *mycer* gene.

Therefore, for at least the reasons presented above, *Nakafuku* does not disclose the claimed invention.

In the Office Action, Claims 6, 23 to 27, 31 to 35 stand rejected under 35 U.S.C. §103(a) as being unpatentable over *Nakafuku* in view of the publication to Eilers et al. ("*Eilers*") and/or the publication to Evans et al. ("*Evans*"). Applicants respectfully traverse these rejections for the reasons discussed below.

The Patent Office admits *Nakafuku* fails to teach the use of *c-myc* constructs fused to steroid/thyroid hormone receptor ligand binding domains other than the estrogen receptor ligand binding domain. The Office Action relies on *Eilers* to cure this deficiency of *Nakafuku*. In a study of the function of human *myc* gene, *Eilers* describes fusing the hormone binding domain of the estrogen receptor gene or the glucocorticoid receptor gene to the human *myc* gene and

transfecting fibroblasts with the chimeric gene. *Eilers* fails to teach or suggest introducing a *c-myc* construct into mammalian neural precursor cells wherein the *c-myc* construct includes at least a portion of a *c-myc* DNA fused with DNA encoding at least a portion of a ligand binding domain as in the claimed invention. Like Nakafuku, *Eilers* also fails to teach or suggest culturing neural precursor cells in a serum-free medium as recited in Claim 31.

Furthermore, *Eilers* fails to teach or suggest a neural precursor cell line comprising a recombinant DNA construct comprising a receptor ligand-regulated *c-myc* gene, wherein at least about 20% of the cell line is capable of differentiating into neurons upon withdrawal of mitogen as recited in Claim 6. *Eilers* also fails to teach or suggest mammalian neural precursor cells comprising a recombinant DNA construct comprising a receptor ligand regulated *c-myc* gene, and wherein at least about 20% of said mammalian neural precursor cells is capable of differentiating into neurons upon withdrawal of mitogen. Therefore, *Eilers* fails to cure the deficiencies of *Nakafuku*.

The Patent Office admits that *Nakafuku* and *Eilers*, alone or in combination, do not teach or suggest a stable culture of human neural precursor cells as in the claimed invention. The Patent Office relies on *Evans* to cure the deficiencies of *Nakafuku* and *Eilers*. *Evans* provides a general description of the activation of genes by binding of hormones to their respective intracellular receptors. *Evans*, however, does not teach or suggest introducing a *c-myc* construct into the cells, wherein the *c-myc* construct includes at least a portion of a *c-myc* DNA fused with DNA encoding at least a portion of a ligand binding domain as recited in Claim 31. Nor does *Evans* teach or suggest a neural precursor cell line comprising a recombinant DNA construct comprising a receptor ligand-regulated *c-myc* gene, wherein at least about 20% of the cell line is capable of differentiating into neurons upon withdrawal of mitogen as recited in Claim 6. Furthermore, *Evans* fails to teach or suggest mammalian neural precursor cells comprising a recombinant DNA construct comprising a receptor ligand regulated *c-myc* gene, and wherein at least about 20% of said mammalian neural precursor cells is capable of differentiating into neurons upon withdrawal of mitogen. Therefore, *Evans* fails to cure the deficiencies of *Nakafuku* and *Eilers* discussed above.

Accordingly, the combination of *Nakafuku*, *Eilers* and *Evans* fails to teach or discuss every element of the claimed invention.

Moreover, there is no teaching or suggestion to motivate one of ordinary skill in the art at the time of the present invention to combine *Eilers* and *Evans* with *Nakafuku*. A rejection based on a *prima facie* case of obviousness is held improper without a motivation to combine the references. *In re Rouffet,* 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998). Also, it is not enough to simply rely on the level of skill in the art to provide the suggestion to combine references as it appears the Patent Office has done on pages 4 and 5 of the Office Action. *Al-Site Corp. v. VSI Int'l Inc.*, 174 F.3d 1308, 50 USPQ2d 1161 (Fed. Cir. 1999). To support its combination and/or modification of the cited art to arrive at the claimed invention, the Patent Office has applied hindsight reconstruction by selectively piecing together teachings of *Evans* and *Eilers* with the teachings of *Nakafuku* in an attempt to recreate what the claimed invention recites. Of course, as discussed above, without the requisite motivation to combine these teachings, this is clearly improper as being hindsight reconstructive. *See In re O'Farrell,* 853 F.2d., 894, 902-903 (Fed. Cir. 1988).

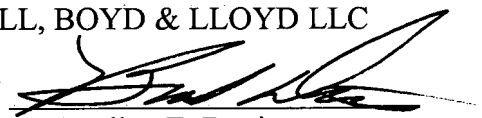
Applicants respectfully submit that the combination of *Nakafuku* with *Evans* and *Eilers* is improper because there is no suggestion or motivation in either reference to combine the references. Furthermore, even if the combination is proper, the references do not teach or suggest all of the limitations of the claimed invention as required to support the present rejection for obviousness. For these reasons the Applicants respectfully submit the obviousness rejection should be withdrawn.

New Claims 39 to 80 are also in condition for allowance for the reasons discussed above.

An earnest endeavor has been made to place this application in condition for allowance and such allowance is courteously solicited. If the Examiner has any questions related to this Response, Applicants respectfully submit that the Examiner contact the undersigned.

Respectfully submitted,

BELL, BOYD & LLOYD LLC

BY 

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